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(STN) Requester's Full Name: Lynda Guo Examiner #: 79756 Date: 12/30/02
Art Unit: 1651 Phone Number 34605-1200 Serial Number: 10/070,018
Mail Box and Bldg/Room Location: 11801-mai/ Results Format Preferred (circle): PAPER DISK E-MAIL
11A1b - office

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Novel target for antiparasitic agents and inhibitors thereof

Inventors (please provide full names): _____

Earliest Priority Filing Date: _____

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Point of Contact:
Mona Smith
Technical Information Specialist
CM1 6A01
Tel: 308-3278

STAFF USE ONLY

	Type of Search	Vendors and cost where applicable
Searcher <u>M. Smith</u>	NA Sequence (#) _____	STN _____
Searcher Phone # _____	AA Sequence (#) _____	Dialog _____
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Date Searcher Picked Up <u>1/2/03</u>	Bibliographic <u>X</u>	Dr. Link _____
Date Completed <u>1/17/03</u>	Litigation _____	Lexis/Nexis _____
Searcher Prep & Review Time <u>60</u>	Fulltext _____	Sequence Systems _____
Clerical Prep Time: _____	Patent Family _____	WWW/Internet _____
Online Time <u>60</u>	Other _____	Other (specify) _____

File 133:MEETING R 1966-1973 Jan WI
File 134:Physics Previews R 1967-1973 Jan WI
File 135:Physics
File 136:PHYSICS OF MATTER Jan
File 137:format only 1973 The Dialog Corp. ratish
File 138:Science & Cited Ref Sci 1974-2003 Jan WI
File 139:format only 1973 Inst for Sci Info
File 140:Dissertation Abs Online 1961-2003 Jan WI
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File 142:SCAR Abstracts 1974-2003 Dec
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File 144:ELSEVIER BIOBASE 1994-2003 Jan WI
File 145:1993 Elsevier Science B.V.
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File 148:JST-HEPlus 1988-2003 Nov WI
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File 150:General Sci Abs Full-Text 1974-2003 Jan
File 151:1993 The HW Wilson Co.
File 152:Pastoral CPTs-2003 Jan WI
File 153:format only 1973 CNRS
File 154:TSD HealthyWellness DB (SM) 1976-2003 Dec WI
File 155:1993 The Gale Group
File 156:TEKFILE 1985-2003 Nov WI
File 157:format only 1973 The Dialog Corporation.
File 158:CAB Health 1983-2003 Dec
File 159:2003 CAB International
File 160:Ecological Record Online(R) 1978-2002 Dec
File 161:2002 BIOSIS
File 162:CLAIMS(R)/US Patent 1950-03/Jan 14
File 163:2003 IFI/CLAIMS(R)
File 164:Derwent WPI 1963-2002/US,UM &UP=200303
File 165:2003 Thomson Derwent
File 166:Derwent Biotech Res. 1982-2003/Jan WI
File 167:2003 Thomson Derwent & ISI
File 168:Current Biotech Abs 1993-2002 Dec
File 169:2002 DEchema
File 170:SciSearch(R) Cited Ref Sci 1974-1987 Dec
File 171:1995 Inst for Sci Info
File 172:Current Contents Search(R) 1991-2003 Jan 14
File 173:2003 Inst for Sci Info

Set	Items	Description
S1	46965	(PARASIT? OR FUNG? OR BIOCID? OR INSECT? OR BACTER?) AND (- SCREEN? OR ASSAY? OR TEST?) AND (PHOSPHATE? OR PHOSPHATASE?)
S1	35477	S1 AND ENZYME? S. INHIB? OR SUPPRESS?
S1	17444	S1 AND ENZYME? S. ACTIVE? OF INHIB? OR SUPPRESS?
S1	917	S3 AND (WORM? OR PROTOZOA? OR NEMATODE? OR MITE?)
S1	570	PI - unique items
S1	11	S1 AND (TERHALOCHEM. 6 - P. GLYPHEROL W. 6 OR MAMMATH. W. 1 - P. P. FRITOL W. 6. W. 1) (PHOSPHATE?)
S1	11	PI - unique items

and I have been told that the
same is the case. Previous to
the time of the last election,

19-1076-2 PHYSICIAN: 2011004787
19-1076-2 PHYSICIAN: 2011004787

AUTHOR: Bressler, Jerome J.; Dale, Lawrence; Hough, Michaela L.; Pucher, Frederick J.; Van, William Wesley; Verlinde, Christianne L. M. J.; Hall, William J.; Hall, Michaela H. A.

AUTHOR ADDRESS: Department of Chemistry, University of Washington, Seattle, WA, United States; e-mail: hall@u.washington.edu

AUTHOR ADDRESS: Department of Medicinal Chemistry, 1959 NE 45th, Seattle, WA, United States

ARTICLE SUBJECT

ARTICLE SUBJECT

ARTICLE TYPE: Abstract

LANGUAGE: English

LANGUAGE: English

ABSTRACT: As part of a project aimed at structure-based design of nucleoside analogues as drugs against African trypanosomiasis, N6-, N2-, and N6,N2-disubstituted adenosine analogues were synthesized and tested in molecular structure-activity relationships for inhibiting Trypanosoma brucei glycosomal phosphoglycerate kinase (PGK), glyceraldehyde-3-phosphate dehydrogenase (GAPDH), and glycerol-3-phosphate acyltransferase (GPT). Evaluation of X-ray structures of parasite PGK, GAPDH, and GPT complexed with their adenosyl-bearing substrates led us to generate a series of adenosine analogues which would target all three enzymes simultaneously. There was a modest preference by PGK for N6-substituted analogues bearing the 2-amino group. The best compound in this series, 2-amino-N6-(2'-p-hydroxyphenyl)ethyl-adenosine (4tb), displayed a 13-fold improvement over adenosine with an IC50 of 1.11 μM. N6-(2'-p-Hydroxyphenyl)ethyl)amino adenosine (4tc) was a weak inhibitor of *T. brucei* PGK with an IC50 of 500 μM. To explore the potential of an additive effect that having the N6 and N2 substitutions in one molecule might provide, the best ligands from the two series were incorporated into N6,N2-disubstituted adenosine analogues to yield N6-(2'-phenylethyl)-2-(2'-phenylethyl)amino adenosine (6b) as a 31 μM inhibitor of *T. brucei* PGK which is 11-fold more potent than the additive template. In contrast, these series gave no compounds that inhibited parasitic GAPDH or GPT more than 10-20% when tested at 1.1 μM. A 3.0 Å NGX-ray structure of a *T. brucei* PGK/4cb complex revealed a binding mode in which the nucleoside analogue was flipped and the ribosyl moiety adopted a syn conformation as compared with the previously determined binding mode of ADP. Molecular docking experiments using QM and SAS program suites reproduced this "flipped and rotated" binding mode.

2000

ABSTRACT FROM: Item 2 from file: 3.
BIOASSAY File: 5:Biosis Previews®
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ABSTRACT: BIBREF ID: 1110004467
AN IMPROVED PURIFICATION OF GLYCOLIPIDASE PP FROM THE SP. CYTOMI TRYPSOMANTIS TMA
A. TAYEBI, J. M. BRUNEAU

AUTHOR: AYANI, P. A.; WANG, C. T.

AUTHOR: ALIREZAI, ARI, MEL. MIRABEYGI, SARAFI, SHIRIN, JOSH. MEF., JAHANGIR, M.,

IRAN.

ABSTRACT: M. J. BIOCHEM PARASITOL 21: 3-12, 1996. Article ID: 1110004467

Full Text Name: Molecular and Biochemical Parasitology

Journal: M. J. BIOCHEM

ARTICLE TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: The glycosomes of *Trypanosoma brucei* and *T. brucei* subsp. *sudanicum* were purified by three different procedures and the results compared by electron microscope, enzyme assays and SDS-PAGE. In *T. brucei* subsp. *sudanicum* glycosomes contain a 10S ribosomal subunit. Purification followed by a sucrose gradient centrifugation resulted in the least purified glycosome preparation. Purification on a pre-formed Nytronium gradient gave an improved preparation of the most homogeneous preparation. In *T. brucei* glycosomes was purified after centrifugation on two successive sucrose gradients. Glycosomes purified by both the Nytronium and sucrose sucrose gradient procedures appeared larger than *in situ* glycosomes, presumably due to the effect resulting from disruption of the granular matrix of the organelles. Nevertheless, there appears to be no loss of cytosolic enzymes due to the swelling of the organelles. The glycosomes of the blood stream form trypomastigotes purified by the same procedure remain, however, no size of swelling. A comparison of glycosomes purified from glycosomes and bloodstream form trypomastigotes prepared by the same double sucrose procedure demonstrates that the glycosomes in procyclic trypomastigotes: 1. activities of new kinase, phosphoglucomutase isomerase, phosphofructokinase, aldehyde and 2. 3-phosphoglycerate kinase and diminished by 1-10%; 2. activities of aldehydeshiftaldehyde- α -phosphate dehydrogenase, triose phosphate isomerase and glycerol-3-phosphate dehydrogenase remain unchanged or are only slightly reduced; 3. there is an appearance of four major new proteins, among which could be phosphoenol pyruvate carboxykinase and malate dehydrogenase. These observations are in basic agreement with those by Hart et al. (Mol. Biochem. Parasitol. 19, 25-35, 1984).

1984

TABLE 3 (Item 3 from file: 5)
 FILE: 5:Biogenesis Previews.R
 © 1984 BIBLIS. All rights reserved.

DOI: 10.1007/BF019466

CHARACTERIZATION OF MALATE DEHYDROGENASE EC-1.1.1.37 ALDOLATATE KINASE EC-2.7.4.3 AND GLYCOLYTIC ENZYMES IN GLYCOSOMES AND THE THREONINE PATHWAY IN THE MITOCHONDRION OF CULTURED PROCYCLIC TRYPOMASTIGOTES OF *TRYPANOSOMA-BRUCEI*

AUTHOR: OEFFENBERG F B; MARKOS A; STEIGER B F

AUTHOR ADDRESS: RESEARCH UNIT FOR TROPICAL DISEASES, INTERNATIONAL INST. FOR CLINICAL AND MOLECULAR PATHOLOGY, ICP, AVENUE HIPPOCRATE 74, B-1160 BRUSSELS, BELGIUM.

JOURNAL: MOLEkul. BIOCHEM. PARASITOLOGY 4 (5-6), 1981 (RCG), 1981, 231-244, 1981

FILE: JOURNAL NAME: Molecular and Biochemical Parasitology

JOURNAL: MRIPB

FILE: TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Procyclic culture forms of the human and cattle parasite *T. brucei* stock 427 were screened for the presence of enzymes involved in glycolysis, mitochondrial energy metabolism and threonine degradation. The enzyme activities in the procyclics were compared with those of the blood stream forms. The specific activities of glycolytic enzymes represented 21-71% of the respective levels in the bloodstream form, except for new kinase (EC 2.7.1.11) which was 21-fold reduced. This finding indicates that the enzymes involved in the early stages of the glycolytic pathway, i.e., fructose kinase, fructose-1,6-diphosphatase, 3-phosphoglycerate kinase and the enzymes NAD+-linked glycerol-3-phosphate

glyceraldehyde-3-phosphate dehydrogenase, and glycerol kinase were all present in glycosomes equilibrating at a density of 1.143 g/ml in sucrose gradients. Malate dehydrogenase was 6-fold more active in procytoblasts than in glycosomes from fibroblasts. This increase in activity was the result of the appearance of malate dehydrogenase in the glycosomes of the procytoblasts, in addition to mitochondrial and cell-sap activities which were present in both states of the little cycle. Glycosomes contained part of the propionate kinase activity, which was also associated with the cell-sap. Malate dehydrogenase (EC 1.1.1.31), and sn-glycerol-3-phosphate dehydrogenase (EC 1.1.1.31), together with 3,3'-dihydroxybenzoate ATPase (EC 3.6.1.3), were located in the mitochondria which had a density in sucrose ranging from 1.14-1.17 g/ml. This organelle also contained L-threonine β -dehydrogenase (EC 1.1.1.1) and carnitine acetyltransferase (EC 2.3.1.1), 2 enzymes involved in threonine catabolism. The latter 2 enzymes had activities which were, respectively, 16- and 18-fold higher in the procytoblasts than in the bloodstream form. Mitochondrial sn-glycerol-3-phosphate dehydrogenase was decreased 4-fold.

1981

TABLE 4 Item 4 from file: 5.
DIALOG FILE 5: Biosis Previews (R)
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108186 BIOSIS NO.: 000069026084
TREHALOSE 6-PHOSPHATE SYNTHASE EC-2.4.1.15 FROM
DICTYOSTELIUM-DISCOIDEUM PARTIAL PURIFICATION AND CHARACTERIZATION OF THE
ENZYME FROM YOUNG SCROCARPS
AUTHOR: KILLICK K A
AUTHOR ADDRESS: DEP. DEV. BIOL., BOSTON BIOMED. RES. INST., BOSTON, MASS.
02114, USA.
JOURNAL: ARCH BIOCHEM BIOPHYS 196 (1). 1979. 121-133. 1979
FULL JOURNAL NAME: Archives of Biochemistry and Biophysics
COUNTRY: AFRICA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Trehalose 6-phosphate synthase was solubilized from young scrocarps of the cellular slime mold, *D. discoideum*, by a freeze-thaw cycle and was subsequently purified about 160-fold using streptomycin sulfate precipitation, (NH4)2SO4 fractionation, DEAE-cellulose chromatography, heat treatment in the presence of heparin and molecular sieve chromatography on columns of Bio-Gel A-1.5 m. The purified enzyme was maximally active at pH 6.5, showed an absolute specificity for G-6-P as glucosyl acceptor and a relative specificity for the glucosyl donor in the order: UDP-glucose, GDP-glucose and ADP-glucose. Although heparin and chondroitin sulfate activated the synthase, the order of glucosyl donor specificity was not affected. Other activators of trehalose 6-phosphate synthase were KCl, Mg2+, and EGTA, while detergents had little effect. Although synthase activity was reduced 41 to 51% upon the omission of Mg2+ from the assay mixture, an absolute dependency for Mg2+ could not be demonstrated. Evaluation of the apparent Km values for partially purified synthase preparations demonstrated that for each of the synthase substrates, the Lineweaver-Burk plots displayed complex biphasic kinetics. Estimation of the Km after extrapolation of the initial rate linear portions of these plots yielded values of 1.1 and 0.1 mM G-6-P and 1.1 and 0.6 mM UDP-glucose. Comparison of the latter parameters with the cellular levels of UDP-glucose and G-6-P in *D. discoideum* suggests that if the observed biphasic kinetics are the consequence of multiple kinetically distinct forms of the synthase, the activation of

Journal of Biological Chemistry, Volume 255, Number 10, April 1980, pp 5100-5104.
© 1980 by the American Society for Biochemistry and Molecular Biology, Inc.

1979

ABSTRACT: Item 5 from file: 5
1979 R-File 5: Biosis Previews R
5 BIOC BIOSIS. All rts. reserv.

2119-BIOSIS NO.: 000064041070
SUBJECT: SURAMIN, SURAMIN AND OTHER TRYPSAN, VIBRIO AND TUBERCLE BACTERIA
OXIDASE AND PHOSPHATE OXIDASE
AUTHOR: FAIRFAX A H; RICKMAN J B F
ADDRESS: DEP. BIOCHEM., UNIV. EDINB., MUR. SCH., EDIN TEL.,
EDINBURGH EH9 9AJ, SCOTL., UK.
JOURNAL: EXP PARASITOL 43 (1977) 383-386, 1977
FULL JOURNAL NAME: Experimental Parasitology
COUNTRY: UK
PUBLICATION TYPE: Abstract
LANGUAGE: English

ABSTRACT: A number of chemotherapeutic compounds effective against *T. brucei* were tested as inhibitors of the purified glycerophosphate oxidase sub-glycerol-3-phosphate oxidoreductase. M-larsenoxine and suramin were potent inhibitors of the dehydrogenase component of this multienzyme complex. Suramin is a potent competitive inhibitor of the oxidase with a K_i of 4.1 μ M with respect to glycerophosphate. The K_m for glycerophosphate for the enzyme decreased from 6.5 to 1.7 μ M in the presence of bovine serum albumin while the V_{max} was increased 2- to 3-fold. Human and bovine serum albumin can protect the oxidase from inhibition by suramin, by preferential binding of the drug. Analogs of suramin with little or no chemotherapeutic value are less effective inhibitors of the oxidase, and the correlation between therapeutic action and potency as inhibitors suggests that this enzyme is likely the principal site of action of suramin *in vivo*.

1979

ABSTRACT: Item 6 from file: 6
1979 R-File 6: Biosis Previews R
6 BIOC BIOSIS. All rts. reserv.

2119-BIOC BIOCIS NO.: 000064041070
A RADIOMETRIC ASSAY FOR TREHALOSE-6-PHOSPHATE SYNTHETASE
PG-24.1.15
AUTHOR: KILNICK K A
JOURNAL: ANAL BIOCHEM 79 (1-2), 1977 300-314, 1977
FULL JOURNAL NAME: Analytical Biochemistry
COUNTRY: ANGLO
PUBLICATION TYPE: Abstract

ABSTRACT: A specific and sensitive radiometric assay was developed for the measurement of trehalose-6-phosphate trehalose-6-phosphate synthetase (EC 4.1.1.11, *Candida utilis* diastaticum) activity. With either ^{32}P -G-1 or ^{32}P -D-glucose as substrate, products unique to the synthetase reaction, i.e., trehalose-6-P and trehalose, may be quantitated after maximal column separation by either density fractionation or phosphorescence. Use of the marker method is valid, and the synthetase activity will not be affected by trehalose-6-phosphate, which is a substrate for phosphatase activity and may result

specificity; and when samples contain no specific antigen, the antibody is applied to a control sample; greater sensitivity and lower levels of false and non-specificity are competing side effects in the search for optimum conditions for assay (e.g., polyacrylamide gel electrophoresis, immunoprecipitation, immunodiffusion, immunofixation, and radioimmunoassay).

John C. Gandy, Jr.,
Chairman, Department of the Arts, University of
Texas at Austin, Austin, Texas, 78712, USA

4001-07 H.W. Wilson Record Number: 30010007
Bibliography of substances and intermediates in polymers and polymerization. Part 1, Part 1, Ring.
Hollings, Hazel M; Haussel, Frank H
Annual Review of Polymer Chemistry, Vol. 1, 1970, pp. 1-477
JOURNAL PREVIEW: 1970-11, ISSN: 0003-4004
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
COUNTRY OF USE: United States

ABSTRACT: The three-dimensional structures of tryptophan synthase, carbamoyl phosphate synthetase, glutamine phosphoribosylpyrophosphate amidotransferase, and asparagine synthetase have revealed the relative locations of multiple active sites within these proteins. In all of these polyfunctional enzymes, a product formed from the catalytic reaction at one active site is a substrate for an enzymatic reaction at a distal active site. Reaction intermediates are translocated from one active site to the next through the participation of an intermolecular tunnel. The tunnel in tryptophan synthase is 15 similar to 15 Å in length, whereas the tunnel in carbamoyl phosphate synthetase is nearly 100 Å long. Kinetic studies have demonstrated that the individual reactions are coordinated through allosteric coupling of one active site with another. The participation of these molecular tunnels is thought to protect reaction intermediates from coming in contact with the external medium. Reprinted by permission of the publisher.

7/AB-1 Item 2 from file: 981
1 ANALOG A File #1:General Sci Abs/Full-Text
2 © 1998 The W. W. Wilson Co. All rights reserved.

4108282 H.W. WILSON RECORD NUMBER: BGS199100282
Experimental evolution and its role in evolutionary physiology.
Pernetti, Albert F
Lerski, Richard E
American Naturalist (Am. Nat.) v. 139 no. 1 (Apr. 1992) p. 146-62
JOURNAL FEATURES: vols. 1-131 ISSN: 0003-0147
LANGUAGE: English
COUNTRY OF PUBLICATION: United States
COUNTRY OF USE: United States

ABSTRACT: Four general approaches to the study of individual-level plasticity in polyphyletic metazoan-based communities, namely, analysis of community assembly, phenotypic plasticity and dispersal, and phylogenetic conservatism, are discussed. We provide an example of the utility of the approach of laboratory selection experiments to study the role of dispersal in environmental adaptation, differences in adaptive potential of generalists and specialists. A niche of the benthic foraminifer *Reticularia* was maintained in a constant environment in the laboratory and was regulated

and 100% survival and allowed to vegetate for 10 weeks. This is a standard, short-term, alternating treatment protocol for cold tolerance studies. The primary objective of this study was to determine the relationship between cold tolerance, as measured by survival, and cold tolerance in the membrane lipids. A secondary objective was to determine the relationship between cold tolerance and the degree of unsaturation in the membrane lipids. The third objective was to determine the relationship between cold tolerance and the degree of saturation of the membrane lipids. Reprinted by permission of the author.

AP 10 Item 1 from file: 149
MAIL TO FILE 149:700 HealthWellness JG.JM
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ALLIED SUPPLIER NUMBER: 94071601 UNE P 80007 018-014-001-001
Changes in membrane polar lipid fatty acids in Seashore paspalum at
resistance to low temperature exposure. Tifgrass (Linen).
Wynne, D.J.; Howell, S.L.; Duncan, R.K.; Baird, W.W.
Crop Science, Vol. 27, 1981 71
N.Y.U.

PUBLICATION FORMAT: Magazine Journal; Subject: ISSN: 0011-183X
LANGUAGE: English; RECDR TYPE: Fulltext; Abstract: JAPORT AMERICAN:
Academic; Trade
WORD COUNT: 6817 LINE COUNT: 30600

AUTHOR ABSTRACT: Seashore paspalum (*Paspalum vaginatum* Sw.) is a winter-season turfgrass, best known for its superior salt tolerance. Plants are subject to injury during winter conditions along the northern boundary of their zone of adaptation. New cultivars that are more tolerant to low temperatures are needed for use in the transition zone. Cold tolerance has been correlated with the degree of unsaturation in membrane lipid fatty acids. Unsaturated fatty acids are thought to aid in maintaining membranes in a fluid state necessary for biological functioning (homoeostasis). The primary objective was to characterize fatty acid composition of membrane lipids in three genotypes differing in cold tolerance. A second objective was to investigate changes in fatty acid content in these genotypes during exposure to low temperatures.

Cold-treated plants were exposed to a 16-h photoperiod at 5 degrees/14 degrees C day/night temperatures and light intensity of 400 micro mol m⁻² s⁻¹ photosynthetic photon flux density for 3 wk. Shoots and crowns were harvested at 7-d intervals. Total lipids were extracted and the polar lipids separated by thin-layer chromatography. Fatty acids were identified by gas chromatography (GC) and mass spectroscopy. In all three genotypes, the two saturated fatty acids, palmitic acid and stearic acid, did not change during cold treatment. The monounsaturated linoleic acid increased significantly during low temperature exposure. The magnitude of change was greater in the fully-textured and more cold-tolerant PI 811111 'Smalsle' than in the intermediate cold-tolerant 'Adalayz' or in the cold-susceptible, semi-textured PI 149142. These findings suggest that accumulation of linoleic acid partly explains the differential response in their cold tolerance.

AP 10 Item 1 from file: 351
MAIL TO FILE 351:Berwent WPI
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AP 10
MAIL TO FILE 351:49-11-001-001

Related WPI Appl No: 2-165114

KRAM Appl No: 2-16437

ABSTRACT: Substrate inhibitors of sugar/sugar alcohol phosphatases and methods for isolating and identifying such inhibitors comprising the following steps:

Patient Ass. Name: IFTIYEH FERGUSON LEWIN

Inventor: THURIFERIN IVAN LICKY

Number of Inventors: 1

Patient Family:

Patient No: Filing Date: Application No: Filing Date: World
KRAM, I. I. All 1987-07-10 1987-07-10 A 165114, 16437, 16438

Priority Applications: No (Type/Date): EP 010000000000

Patient Details:

Patient No: FERGUSON FERGUSON LEWIN

KRAM, I. I. All 1987-07-10

Isolated substrates for sugar alcohol : AI AT EP 010000000000 IF A 165114 EP 010000000000 IF A 16437 EP 010000000000 IF A 16438

Assignee: FERGUSON, IAN, IFTIYEH, I.

Assignee: FERGUSON, I.

INVENTION - Assessing substances as novel enzyme inhibitors of sugar alcohol phosphatases in cells where the sugar/sugar alcohol accumulates e.g. stress or abnormal conditions comprises:

- Measuring the enzyme activity in the presence of the inhibitor and sugar/sugar alcohol phosphate in a biological medium; and

- Determining that the substance is an inhibitor if the enzyme activity is reduced.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an inhibitor obtained by the method of the invention.

ISM - The method is used to isolate inhibitors of sugar/sugar alcohol phosphatases and lead to a cytotoxic build up of an intermediate normally produced under conditions of stress claimed. The inhibitor can be used as a cicidic along with an antifungal agent e.g. an article claimed.

ADVANTAGE - The inhibitors have a novel mechanism of action compared to known anti-fungals and would therefore be less likely to encounter resistance among pathogenic fungi. Known antifungals often have undesirable side-effects e.g. toxicity to mammalian cells which would not be encountered with the new inhibitors.

pp: 29 DwgNo: C/9

7/AB/01 Item 2 from file: 651.

SEARCHED, FILED 15/1/2001: Ferwent WPI

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111000000000

WPI Appl No: 2000-235114/200114

Related WPI Appl No: 2000-246403

KRAM Appl No: 2-16437

New inhibitors and screening assay for inhibitors or suppressors of sugar alcohol phosphatases for sugar phosphatases

Patient Ass. Name: IFTIYEH FERGUSON LEWIN

Inventor: THURIFERIN IVAN LICKY

Number of Inventors: 1 Number of Patents: 1

Patient Family:

Patient No: Filing Date: Application No: Filing Date: World
KRAM, I. I. All 1987-07-10 1987-07-10 A 165114, 16437, 16438

Assignee: FERGUSON, IAN, IFTIYEH, I. All 1987-07-10 1987-07-10

Patient No: Filing Date: Application No: Filing Date: World
KRAM, I. I. All 1987-07-10 1987-07-10 A 165114, 16437, 16438

1. *Leucosia* (Leucosia) *leucosia* (L.) (Fig. 1)

1. *See* *W. H. H. Clayton, The English Poor Law, 1834-1939* (London, 1960).

10. *W. C. R. Smith, 1990, The role of the *liver* in the metabolism of *nitrogen* in *fish*, *Review*, *Environ. Biol. Fish.*, **28**, 111-128.*

United States Report of the Secretary of State, 1860, p. 111.

ANSWERING THE CALL: THE CHURCH AND THE CHINESE

THE BOSTONIAN 11

NUCLEOLY - A screening assay for inhibitors or suppressors of sialyl alcohol phosphatases or sugar phosphatases using enzymes from *Yeast*, *Bacillus*, *Insects*, *Neurofibromas*, *Mice* or *Human Cells*, see p. 29.

1. PRACTICAL DEFINITION - A method for assessing the activity of test substances as inhibitors of a first cell enzyme converting a sugar phosphate into a sugar, or a sugar alcohol (glucoside) into a sugar alcohol in cells. The sugar or sugar alcohol is accumulated in large quantities by the cells, e.g. under conditions deviating from the optimal growth condition of the target cells or is a result of stressed conditions, the inhibition being directly of the first enzyme or indirectly. The method comprises:

a contacting a test compound with a biological medium comprising the sugar phosphate or sugar alcohol phosphate and the sugar alcohol;

by measuring the activity in the medium which depends on the activity of the first enzyme;

(c) repeating steps (i) and (2), with further test compounds; and
 (d) selecting at least 1 compound which reduces activity of the
 enzyme compared with the same medium without the inhibitor; and
 (e) (optionally) assessing the activity of a second cell enzyme
 which is involved in the synthesis of the corresponding sugar
 thiofuran or sugar alcohol phosphate.

The selecting step includes selection of inhibitors which reduce the activity of the first enzyme while maintaining a viable activity of the second enzyme.

INDEPENDENT CLAIMS are not included for the following reason:

Inhibitors Identified by the MDM2 Assay

is a boricide acting on fungi, viruses, nematodes, bacteria or other organisms accumulating large quantities of sugar.

4. a method of increasing the sugar phosphate or sugar aldehyde phosphate content in a target cell, particularly a mammalian cell, comprising using an inhibitor to reduce the activity of a first cell enzyme converting a sugar phosphate into a sugar or sugar aldehyde phosphate, and a sugar aldehyde.

is a means of reducing or impairing the pathogenicity of a mammalian parasite by promoting hyperplurulation at a site of implantation in a single animal host.

ANTIMITE = Antiparasitic; INHIBITOR = Inhibitor of protein synthesis; PROTEIN STABILIZER = Protein stabilizer.

¹² See, for example, the discussion of the 1992 Constitutional Convention in the *Constitutional Convention of 1992* (1993).

III. Results

For the determination of α and β values were applied the classical polymer techniques, and from the α value by analogy the β was calculated. The compound III had an α of 0.011 at the power $\omega = 20$.

This is the result of a rather poor method of determination of the mechanical properties, particularly of rubber, because the α value is not the true value, it is a result from a different method of measurement, i.e., it is a shear, allene, or β value.

It is shown in

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FILE COVERS 1907 - 17 Jan 2003 VOL 148
FILE LAST UPDATED: 16 Jan 2003

This file contains CAS Registry Number: to easily and accurately substance identification.

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=> d stat que
L1      39 SEA FILE=REGISTRY TREHALOSE-4-PHOSPHATE?/CN
L2      195 SEA FILE=REGISTRY GLYCOPHOSPHATE?/CN
L3      23 SEA FILE=REGISTRY MANNOSPHOSPHATE?/CN
L4      5 SEA FILE=REGISTRY SORBITOL-6-PHOSPHATE?/CN
L5      1 SEA FILE=REGISTRY ERYTHROSE-4-PHOSPHATE?/CN
L6      1 SEA FILE=REGISTRY SUGAR PHOSPHATE?/CN
L7      14 SEA FILE=REGISTRY SUGAR PHOSPHATE?/CN
L8      325 SEA FILE=HCAPLUS L1 OR SUGAR PHOSPHATE?/CN
L9      5869 SEA FILE=HCAPLUS L2 OR SUGAR PHOSPHATE?/CN
L10     231 SEA FILE=HCAPLUS L3 OR SUGAR PHOSPHATE?/CN
L11     113 SEA FILE=HCAPLUS L4 OR SUGAR PHOSPHATE?/CN
L12     11 SEA FILE=HCAPLUS ARABITOL-6-PHOSPHATE?/CN
L13     96 SEA FILE=HCAPLUS ERYTHROSE-4-PHOSPHATE? OR L6
L14     3083 SEA FILE=HCAPLUS L7 OR SUGAR PHOSPHATE?/CN
L15     6996? SEA FILE=HCAPLUS (?PARASITE? OR FUNG? OR BIOSID? OR ?INSECT?)  
AND (SCREEN? OR ASSAY? OR TEST?/CN)
L16     10036 SEA FILE=HCAPLUS PHOSPHATASE? OR SUGAR(W) PHOSPHATASE?  
E? OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14
L17     71 SEA FILE=HCAPLUS L15 AND L16
L18     52 SEA FILE=HCAPLUS L17 AND L18 AND?
L19     15 SEA FILE=HCAPLUS L18 AND L19 AND? OR BACTER? OR PROTOZOA? OR  
NEMATODE? OR MITE?
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=> d fibib abs nitro 119 1-1

L19 ANSWER 1 CF 15 HCAPLUS COPYRIGHT 2003 ARI
ACCESSION NUMBER: 2002:645786 filed 07/17/02
DOCUMENT NUMBER: 137:226941
TITLE: Use of certain cytokines for treatment of a number of
conditions including blood cell deficiencies
INVENTOR(S): Ahlem, Clarence L.; Beading, Christopher; Frincke,
James; Stirkha, James; Lardy, Henry; Marwah, Padma;
Marwah, Asma; Hollis-Eden, Patrick T.
PATENT ASSIGNEE(S): Hollis-Eden, Patrick T.; Lalls, Inc., USA

SOURCE: PCT Int. Appl. 136:156403
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002169878	A1	20021011	02-US6716	20010511
W: AE, AG, AL, AM, AT, AU, AR, BE, BG, BR, BY, BA, CA, CH, CN, CO, CR, CU, DE, DK, DM, DZ, EE, ES, FI, GB, GR, GE, GH, GM, HR, HU, ID, IL, IM, IS, IT, KE, KG, KP, KR, KZ, LS, LK, LR, LS, LT, LV, MA, MD, ME, MN, MX, NY, ME, NO, NL, OM, PH, PL, PT, RC, RU, SD, SE, SI, TR, TM, TN, TR, TT, TZ, UA, UG, VE, VN, YU, BA, DE, DK, AE, BY, KG, KG, ME, RU, TZ, TM				
RW: GH, GM, BE, IS, MX, ME, DZ, EE, ES, FI, GB, GR, GE, GH, CY, DE, DK, ES, PT, FR, IT, IS, LT, LV, ME, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, DZ, EE, ES, FI, GB, GR, GE, GH, ME, NL, PT, SE, TR, TZ				
PRIORITY APPLN. INFO.:			1-272624P	P 20010501
			1-320483	P 20010523
			1-323016P	P 20010910
			1-328738P	P 20011011
			1-340354P	P 20011101
			1-338015P	P 20011108
			1-343523P	P 20011220

OTHER SOURCE(S): MARPAT 136:27477

AB The invention relates to the use of compounds to treat a no. of conditions, such as thrombocytopenia, neutropenia, or the delayed effects of radiation therapy. Compsd. that can be used in the invention include methyl-2,3,4-trihydroxy-1-O-(7,17-dihydro-5-ene-3.beta.-yl)-.beta.-D-glucopyranosid ronate. Formulations of the steroids are also exemplified.

IT 9075-65-4, Glycerocephosphate dehydrogenase
 RL: BSU (Biological study, unclassified); BICL (Biological study) (steroid hormone induction of the rate of mitochondrial GDPH and cytosolic malic enzyme in rat liver); synthetic prepn. and use of certain steroids for treatment of a no. of conditions including blood cell deficiencies)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. 13 CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 15 HCPLUS COPYRIGHT 2002 AIG

ACCESSION NUMBER: 2002:89878 H 136:156403
 DOCUMENT NUMBER: 136:156403
 TITLE: Methods for identifying therapeutic targets for treating infectious disease
 INVENTOR(S): Shepard, Michael J.; Hackey, David B.; Cathers, Brian E.; Sergeeva, Nadezhda
 PATENT ASSIGNEE(S): Newbiotics, Inc.
 SOURCE: PCT Int. Appl. 136:156403
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001094561 A1 20010916161 11-07-2001
 W: AE, AG, AL, AM, AT, AU, AZ, BY, BR, BG, BE, BY, BG, CA, CH, CN, CR,
 CZ, DE, DK, DM, EE, ES, FI, GR, IE, IR, IS, CN, CH, CM,
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KW, MN, NL, LC, HK, LP, IS, LT, LV,
 MA, MD, MG, MK, MN, MW, MA, NL, PL, PT, RC, RU, SE, SG,
 SI, SK, SL, TM, TR, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
 RM, AZ, BY, KG, KZ, MD, PT, TZ, VN
 RW: GH, GM, KE, LS, MW, MZ, SL, TZ, UG, TZ, VN, AT, BE, CH, CY,

PRIORITY APPLN. INFO.:

-11-07-2001

-24498386 11-07-2001

1-3967235 11-07-2001

AB This invention provides methods and compositions to identify **enzymes** that act as **enzyme**-catalyzed therapeutic activators and the **enzymes** identified by these methods. The compounds provided by this invention are compds. activated by the **enzymes** as well as compns. contg. these compds.

IT 37250-69-4

RI: BSL (Biological study); unclass.; CAT (Catalyst use); THU (Therapeutic use); BIOL (Biological); USES (Uses); (identifying intrinsic **enzyme**-catalyzed therapeutic activators as targets for treatment of a disease).

IT 9025-72-3, E.C. 3.1.3.12

RI: CAT (Catalyst use); PRP (Proprietary); THU (Therapeutic use); BIOL (Biological study); USES (Uses); (identifying intrinsic **enzyme**-catalyzed therapeutic activators as targets for treatment of a disease).

L19 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 1999-2003

ACCESSION NUMBER: 2101:845255 11-07-2001

DOCUMENT NUMBER: 136:34648

TITLE: Genes, **enzymes**, related intermediates, and methods for analysis of mevalonate-independent isoprenoid biosynthesis pathway

INVENTOR(S): Aiam, Petra; Bock, Auelbert; Eisenreich, Wolfgang; Fellermeier, Michael; Hecht, Stefan; Rohdich, Felix; Schuh, Christopher; Wungsintawekul, Juraithip; Jenk, Meinhard H.

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 1-11-01.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10027821	A1	20011026	10027821-10027821	20010605
WO 2001094561	A2	20011026	0101-EP6258	20010601
WO 2001094561	A3	20010631		
W: AE, AL, AM, AT, AU, AZ, BY, BR, BG, BE, BY, BG, CA, CH, CN, CR, CZ, DE, DK, DM, EE, ES, FI, GR, IE, IR, IS, CN, CH, CM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KW, MN, NL, LC, HK, LP, IS, LT, LV, MA, MD, MG, MK, MN, MW, MA, NL, PL, PT, RC, RU, SE, SG, SI, SK, SL, TM, TR, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, RM, AZ, BY, KG, KZ, MD, PT, TZ, VN RW: GH, GM, KE, LS, MW, MZ, SL, TZ, UG, TZ, VN, AT, BE, CH, CY,				

SE, DK, ES, FI, FR, GR, HU, I, IL, MD, NL, PT, SE, TF, BF,
BJ, CF, CG, CI, CM, GA, GR, HU, MR, NE, SN, TZ, TS

PRIORITY APPLN. INFO.:

The present invention concerns **enzymes** and intermediates of the mevalonate-independent isoprenoid biosynthesis pathway downstream from 2C-methyl-D-erythritol-2,4-cyclophosphate, i.e., upstream from isopentenylpyrophosphate or dimethylallylpyrophosphate. These are used for screening for inhibitors of the **enzymes** and for identification of inhibitor-resistant variants. Further disclosures concern genes coding for the **enzymes**, vector constructs containing the genes, cells which contain the vectors, and plasmids containing such vectors. Thus, the *Bacillus subtilis* and *Escherichia coli* genes for the mevalonate-independent isoprenoid biosynthetic pathway were cloned and expressed. The DMP synthase and DXP reductoisomerase **enzymes** were used to prep. [^{14}C -13C]-2C-methyl-D-**erythritol-4-phosphate**. The gene *ydiE* 1-deoxy-D-xylulose-5-phosphate reductoisomerase, gene *yaeM* 1-deoxy-D-xylulose-5-phosphate synthase, and gene *ygbP* 4-diphosphocytidyl-2C-methyl-D-erythritol synthase were used in prepns. of [$^{12,2-13C_2}$]-4-diphosphocytidyl-2C-methyl-D-**erythritol**. Genes downstream of *ygbP*, i.e., *gspE*, *lytB*, *yieE*, and *lytC* were cloned for use in screening for inhibitors of isoprenoid biosynthesis or for prep. intermediates in the pathway.

L19 ANSWER 4 OF 15 MCAPLUS COPYRIGHT 1993

ACCESSION NUMBER: 2001:816926 H11017

DOCUMENT NUMBER: 135:354706

TITLE: Structure of 4-diphosphocytidyl methylerythritol synthetase involved in mevalonate-independent isoprenoid biosynthesis and the rational design of effectors

INVENTOR(S): Noel, Joseph L.; Human, Marianne E.; Richard, Stephane

PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, USA

SOURCE: PCT Int. Appl., 1993.

CODEN: PIXXDB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WC 2001033769	A2	20011108	W 2001-US14371	20010503
WC 2001033769	A3	20020829		
W: AE, AG, AL, AM, AT, AU, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KR, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MT, MN, MX, MZ, NC, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TM, TR, TT, TZ, CA, CG, US, CZ, VN, YU, ZA, ZW, AM, AZ, BY, DE, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SL, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, HU, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GR, HU, MR, NE, SN, TZ, TS				
PRIORITY APPLN. INFO.:			-2001033769 P	20010503
			-2001033769 P	20011121a

AB The present invention provides the structure of the **enzyme** 4-diphosphocytidyl-2C-methylerythritol synthetase, a member of the cytidyltransferase family of **enzymes**. ^{14}C -DMP is a crit.

intermediate in the mevalonate-independent pathway for isoprenoid biosynthesis in a no. of prokaryotic organisms, in algae, in the plastids of plants, and in the malaria **parasite**. Since vertebrates synthesize isoprenoid precursors via the mevalonate pathway, FPP-ME synthase and other **enzymes** of the mevalonate-independent pathway for isoprenoid precursors represent attractive targets for the structure-based design of selective antiparasitic, antiviral, and antimicrobial drugs. Accordingly, the present invention provides methods for screening for compounds that inhibit **enzymes** of the mevalonate-independent pathway and pharmaceutical compounds and pharmaceutical formulations thereof. Further provided are methods of controlling the **enzymes** of the pathway and **bacterial** terpenoid synthases, and methods for treating a subject suffering from a bacterial infection.

119. ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2001-2007
 ACCESSION NUMBER: 200116357 WO 20011129
 DOCUMENT NUMBER: 134:217145
 TITLE: Sugar alcohol ester phosphatases or sugar phosphatases as novel targets for antiparasitic agents and use of the inhibitors in biocides and pharmaceuticals
 INVENTOR(S): Thevelein, Janusz; Mifick, Patrick
 PATENT ASSIGNEE(S): K.U. Leuven Research & Development, Belg.
 SOURCE: PCT Int. Appl., 2001-08-29
 CODEN: PIXX02
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016357	A2	20010308	134:217145-EP8410	20000829
WO 2001016357	A3	20011129		
	W:	AE, AG, AL, AM, AT, AU, A, B, BE, BG, BR, BY, BX, CA, CH, CN, CR, CU, CZ, DE, DK, DM, D, E, F, FI, GB, GD, GE, GH, GM, HR, HU, IE, IL, IN, IS, JP, KE, NL, NP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MW, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TI, U, V, BR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KU, M, PT, TJ, TM		
	RW:	GH, GM, KE, LS, MW, MZ, SI, U, V, Z, TZ, US, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, I, J, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GM, M, MR, NE, SN, TD, TG		
EP 1081232	A1	20010307	134:217145-1999-202605	19990830
	R:	AT, BE, CH, DE, DK, ES, FR, G, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		
EP 1206569	A2	20020522	134:217145-964054	20000829
	R:	AT, BE, CH, DE, DK, ES, FR, G, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, M, M		
PRIORITY APPLN. INFO.:			134:217145-A	19990830
			-EP8410-A	20000829
			-EP8410-W	20000829

AB The use of an **enzyme** found in fungi, bacteria, insects, nematodes, worms, mites, protozoa etc. as a target in a screening assay is described by means of which a compound capable of inhibiting the function of that **enzyme** may be identified. The screening assay may include complex, crude or purified-enzyme assays. In particular, the invention

related to a screening assay for inhibitors or suppressors of sugar phosphatases, and more in particular, to inhibitors or suppressors of trehalose-6-phosphate phosphatase, as well as preps., in particular, to artificial preps., which include inhibitors or suppressors obtained by screening. Inhibitors are described as novel targets for applications in biocides and antifungal pharmaceuticals.

II 9023-07-8, Sugar phosphatase 9025-72-3
, Trehalose-6-phosphate phosphatase

9055-29-2, Mannitol-1-phosphatase 37228-75-4,
Glycerol-3-phosphatase

RL: BAC (Biological activity or effect, except adverse); BBR (Biological process); BSM (Biological study, method); BSL (Biological study); PROC (Process)

(inhibitors; sugar alc. phosphatases as novel targets for antiparasitic agents and use of inhibitors as biocides and pharmaceuticals)

EPO ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2001

ACCESSION NUMBER: 2000:742235
DOCUMENT NUMBER: 133:291982
TITLE: Modification of lipid biosynthesis by DNA shuffling

INVENTOR(S): Yuan, Ling; Kuo, Li; Sun, Ai; Lassner, Michael

PATENT ASSIGNEE(S): Maxygen, Inc.,

SOURCE: PCT Int. App., 19990410

CODEN: PIXMD

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061740	A1	20001019	00110400-US9265	20010406

W: AE, AL, AM, AT, AU, AZ, BE, BG, BR, BY, CA, CH, CN, CR, CU,
CZ, DE, DK, DM, EE, ES, FI, IL, IS, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, LV, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, N, NL, NO, PT, RO, RU, SD, SE, SG, SI,
SK, SL, TJ, TM, TR, TT, TW, US, UZ, VN, YU, ZA, ZW, AM,
AZ, BY, EG, KZ, MD, RU, T, ZA, ZW
RW: GH, GM, HE, LS, MW, SD, SI, TW, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, I, IL, IS, NO, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, KW, LY, MR, SN, TD, TG

PRIORITY APPLN. INFO.: PCT/US980707 P 19990410

AB Methods of modulating lipid prodn. in cells and whole organisms by DNA shuffling are provided. Single gene, plasmids, lipoproteins, lipid biosynthetic cycles and whole genomes can be recombinantly modified to produce cells and organisms with desirable lipid synthetic or metabolic activity. Libraries of recombinant lipid synthetic nucleic acids and organisms are also provided.

Modification of lipid satn., fatty acyl chain length, location, fatty acid accumulation, compon., acyl chain length, location, fatty acid accumulation, triglyceride yield, substrate specificity, expression level, are described. A decrease in susceptibility to protease cleavage, high or low pH levels, extreme temps., are also described. A decrease in toxicity, and modification of methyltransferases, resulting in formation of branched chain, cyclopropyl, methoxyl, and other fatty acids, are also described. Use of two-hybrid system for detecting the changes in lipid biosynthetic activity is also described. Screening of libraries,

such as phage display library is a powerful tool. Crop plants such as corn, peanut, barley, millet, rice, soybean, cotton, wheat, oats, sunflower, or peanut whose lipid biosynthetic pathway is well characterized, are examined. DNA shuffling is a powerful process to generate a large amount of genetic diversity by recombination, resulting in a large number of mutations from individual genes.

REFERENCE COUNT: 12 THERE ARE 12 REFERENCES AVAILABLE FOR THIS RECORD. A FULL LIST IS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2000
 ACCESSION NUMBER: 2000:6150_HCA
 DOCUMENT NUMBER: 132:307072
 TITLE: The non-photosynthetic isoprenoid biosynthesis of plants as a test system for new herbicides and drugs against pathogenic **bacteria** and the malaria **parasite**

AUTHOR(S): Bischetti, Michael; Biedler, Johannes; Schwender, Jochen; Boller, Christian
 CORPORATE SOURCE: Botanisches Institut (BIO), Universitat Karlsruhe, Karlsruhe, Germany

SOURCE: Zeitschrift fur Naturforschung, C: Journal of Biosciences (1995, v. 50, p. 305-313)
 CODEN: ZNCBDA; ISSN: 0343-5075

PUBLISHER: Verlag der Gesellschaft fuer Naturforschung
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Higher plants and several photosynthetic algae contain the plastidic 1-deoxy-D-xylulose 5-phosphate (α -D-1-deoxy-D-**erythritol** 4-phosphate) pathway (DOXP/MEP pathway) for isoprenoid biosynthesis. The first four enzymes of this pathway are known of this novel pathway. All of these enzymes of this isoprenoid pathway are potential targets for new classes of herbicides. Since the DOXP/MEP pathway also occurs in several pathogenic **bacteria**, such as *Mycobacterium tuberculosis*, and in the malaria **parasite** *Plasmodium falciparum*, it is possible that new herbicides of the DOXP/MEP pathway are also potential drugs against pathogenic **bacteria** and the malaria **parasite**. Plants with their easily to handle DOXP-pathway are thus very suitable test-systems also for new drugs against pathogenic **bacteria** and the malaria **parasite**. In particular security measures are required. It is known, that the antibiotic herbicide fosmidomycin specifically inhibits not only the DOXP reductoisomerase in plants, but also that in **bacteria** and in the **parasite** *P. falciparum*, and cures malaria-like in mice. This is the first successful application of a herbicide against the novel isoprenoid pathway as a possible drug against malaria.

REFERENCE COUNT: 40 THERE ARE 40 REFERENCES AVAILABLE FOR THIS RECORD. A FULL LIST IS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2000
 ACCESSION NUMBER: 2000:6150_HCA
 DOCUMENT NUMBER: 132:307072
 TITLE: Characterisation of the HLA gene located between the Class II region and the H4 genes in the human MHC
 AUTHOR(S): Aguado, P.; Lafferty, B. J.
 CORPORATE SOURCE: MRC Immunology Unit, Oxford University, Oxford, OX1 3QU, UK
 SOURCE: HLA: Genetic Diversity of HLA Functional and Medical Implications, 11th Congress of the International

PATENT ASSIGNEE IS : Association Internationale Immunotherapy Midwest Limited
SOUTH Africa

DOCUMENT TYPE: Patient
PARENTAL: English
PARENTAL NUM. COUNT: 1
PARENTAL NAME: S.

AB This invention presents and claims an **enzyme** which catalyzes the conversion of L-galactonolactone. The **enzyme** is a catalytic conversion is an oxidase. The mature form of L-galactose dehydrogenase from pea is provided. The invention further provides: (1) an **fungi**, algae or mammal) engineered L-galactose dehydrogenase; (2) a L-galactose dehydrogenase gene-specific probe used to monitor gene presence; (3) a diagnostic monitoring method using the L-galactose multi-**enzyme** pathway or method of production, wherein one step is catalyzed by L-galactose dehydrogenase; (4) a dietary supplement comprising ascorbic acid that contains increased levels of a L-galactose dehydrogenase antisense DNA to down-regulate the **enzyme**; and (5) a herbicidal compn. comprising a herbicide that inhibits L-galactose dehydrogenase, plant L-galactose dehydrogenase, L-galactose is dependent and the plant at Cl. The N-terminal sequence of L-galactose dehydrogenase from pea is provided. The invention further provides: (1) a plant, **bacteria**, **fungi**, **algae** or **mammal** that expresses L-galactose dehydrogenase gene-specific probe used to test, assay or monitor L-galactose dehydrogenase polypeptide; (4) a dietary supplement comprising L-ascorbic acid, L-galactose dehydrogenase; (5) a dietary supplement comprising an organism, preferably a plant, that expresses L-galactose dehydrogenase; (6) use of L-galactose dehydrogenase to down-regulate the **enzyme**; and (7) use of the **enzyme** to catalyze the conversion of L-galactose to D-galactose.

REFERENCE COUNT: 62 THERE ARE 62 REFERENCES AVAILABLE FOR THIS
BIOLOGICAL SUBJECT. 62 REFERENCES ARE AVAILABLE IN THE REFORMAT

ANSWER 11 OF 15 NCAP PLUS 38.38% 24.00% 100%

DOCUMENT NUMBER

Friendship & phosphorus phosphatases

prospective cases. The results of this study will be presented at the 1998 Annual Meeting of the American Society of Hematology.

ANTHONY S. COOPER, ROBERT A. HALLER, AND THOMAS J. WILSON

WILHELM, J. VOGEL, GENEVIEVE, ROBERTSON, ROBERT
Heller, Thomas, 1900-1952

CORPORATE SOURCE: Botanisches Institut, Universität Basel, Basel,
CH-4056, Switzerland

SOURCE: Plant Physiology, 119, 103-110, 1999
CITATION: PLOUGH, J. S., et al. 1999 - 411.
PUBLISHER: Blackwell Science
DOCUMENT TYPE: Journal Article
LANGUAGE: English
ABSTRACT: It is currently thought that most higher plants lack the capacity to synthesize trehalose, a common disaccharide found in bacteria, fungi and invertebrates that appears to play a major role in desiccation tolerance. Attempts have been made to render plants more drought-resistant by the expression of bacterial genes for trehalose synthesis. It is demonstrated here that *Arabidopsis thaliana* itself possesses genes for at least one of the enzymes required for trehalose synthesis, **trehalose-6-phosphate phosphatase**. The yeast *tps2* mutant, which lacks this enzyme, is heat-sensitive, and Arabinosid *tp2* cDNA able to complement this effect has been screened for in *Arabidopsis*. The yeast transformants that grew at 37.5°C contained cDNA able to produce trehalose. All of these expressed either the *Arabidopsis* cDNA, either *AtTPPA* or *AtTPPB*, which are identical to the C-terminal part of the yeast *TPS2* gene and other bacterial trehalose-6-phosphate phosphatases. Yeast transformants expressing *AtTPPA* or *AtTPPB* contained **trehalose-6-phosphate phosphatase** activity that could be measured both *in vivo* and *in vitro*. The enzyme dephosphorylated **trehalose-6-phosphate** but not glucose-6-phosphate or sucrose-6-phosphate. Both genes are expressed in flowers and young developing tissue of *Arabidopsis*. The finding of these novel *Arabidopsis* genes for **trehalose-6-phosphate phosphatase** strongly indicates that a pathway for trehalose biosynthesis exists in *Arabidopsis*.

IT 9025-72-3, Trehalose-6-phosphate phosphatase

phosphocase

REVIEW (Properties)

Chloroalose- α -phosphatase phosphatasas from Arabidopsis

phosphatases from *Arabidopsis* and the identification by functional complementation of yeast mutants.

ANSWER TO Q 15 HIGHFLOSS 2014-01-01

ACCESSION NUMBER: 1993:235635 H

DOCUMENT NUMBER: 118:230655

TITLE: Effect of entomopathogenic bacteria on mitochondrial electron activities in the weevil *Sitophilus oryzae* (Lepidoptera:Curculionidae)
AUTHOR (S): Hadiq, I. & M. N. S. E.

AUTHOR(S): Heddi, A.; Lefebvre, J.; Nardon, M.

CORPORATE SOURCE: Lab. Biocell. Appl., 1040 Lyon, Villeurbanne, 69621, Fr.
SOURCE: Insect Biochem. Mol. Biol. Molecular Biology (1993),
23 (3), 473-510
CODEN: IBMBEJ ISSN: 0020-404X

DOCUMENT TYPE: Journal CODEN: TRIBER, ISSN: 0041-7443

DOCUMENT TYPE: JOURNAL
LANGUAGE: English

LANGUAGE: ENGLISH

AB Various mitochondrial enzymes were investigated in symbiotic and aposymbiotic larvae and adults of *Leucania philus* *oryzae*. Six enzymes were assayed: cytochrome *c* oxidase, succinate cytochrome *c* reductase, glycerol 3-phosphate cytochrome *c* reductase, isocitrate lyase, pyruvate dehydrogenase, and α -ketoglutarate dehydrogenase. The specific activities of all these enzymes were higher in mitochondria isolated from symbiotic larvae than those isolated from aposymbiotic larvae. In adults, the differences in enzymatic activities between symbiotic and aposymbiotic

SEARCHED:
INDEXED:
DOCUMENT TYPE:
JOURNAL:
SUBJ:
AB: It is currently thought that most flowering plants have the capacity to synthesize trehalose, a common disaccharide in **bacteria**, **fungi** and invertebrates that appears to play a major role in osmotic tolerance. Attempts have therefore been made to render plants more drought-resistant by the expression of microbial genes for trehalose synthesis. It is demonstrated here that *Arabidopsis thaliana* itself possesses genes for at least one of the **enzymes** required for trehalose synthesis, **trehalose-6-phosphate phosphatase**. The yeast *tps1* mutant, which lacks this **enzyme**, is heat-sensitive, and *Arabidopsis* cDNA able to complement this effect has been **screened** for. Half of the yeast transformants that grew in 37°C were able to grow at 42°C. All of these expressed one of two *Arabidopsis* cDNA, either ACTPPA or ACTPPB, which are both homologous to the C-terminal part of the yeast *TPS2* gene and other microbial **trehalose-6-phosphate phosphatases**. Yeast *tps2* mutants expressing ACTPPA or ACTPPB contained **trehalose-6-phosphate phosphatase** activity that could be measured both *in vivo* and *in vitro*. The **enzyme** dephosphorylated **trehalose-6-phosphate** but not glucose-6-phosphate or sucrose-6-phosphate. Both genes are expressed in flowers and young developing tissue of *Arabidopsis*. The finding of these novel *Arabidopsis* genes for **trehalose-6-phosphate phosphatase** strongly indicates that a pathway for trehalose biosynthesis exists in plants.
9025-72-3, **Trehalose-6-phosphate phosphatase**
RL: PRP (Properties)
"trehalose-6-phosphate phosphatases from *Arabidopsis thaliana*: identification by functional complementation of yeast *tps2* mutant"
ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:230685 HCAPLUS
DOCUMENT NUMBER: 118:230685
TITLE: Effect of endosymbiotic **bacteria** on mitochondrial enzymic activities in the weevil *Sitophilus oryzae* (Coleoptera:Curculionidae).
AUTHOR(S): Hedi, A.; Lefebvre, F.; Nardon, P.
PUBLISHER: Lab. Biol. Appl., INSA Lyon, Villeurbanne, 69621, Fr.
JOURNAL: Insect Biochemistry and Molecular Biology (1993), 23(3), 403-11
CODEN: IBMBES; ISSN: 0966-0444
DOCUMENT TYPE: Journal
LANGUAGE: English
AB: Various mitochondrial enzymic activities were investigated in symbiotic and apsymbiotic larvae and adults of *Sitophilus oryzae*. Six **enzymes** were assayed: cytochrome c oxidase, succinate cytochrome c reductase, glycerol 3-phosphate cytochrome c reductase, isocitrate dehydrogenase, pyruvate:benzoate oxidase and alpha-ketoglutarate dehydrogenase. The specific activities of all these **enzymes** were higher in mitochondrial isolates from symbiotic larvae than those isolated from apsymbiotic larvae. In addition, the differences in enzymic activities between symbiotic and apsymbiotic

insects were contaminated. Malathion-Heptakis was only partially active. Activity was similar in the 2 strains, and pyrethrin, malathion, and heptakis were similar in sp. *Cydia pomonella* strains. From these results, it is evident that **symmetric** and **asymmetric** **insects** are killed similarly, but the presence of **bacteria** in the diet is important for the insect enzymes to function well. It is also evident that some microbial metabolites could be implicated. These compounds are usually **first tested** on **symmetric** **bacteria** to detect their larval **bacteriome**. No activity was seen.

11. ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1982:1043P HCAPLUS

DOCUMENT NUMBER: 116:1043P

TITLE: Target gene-complemented microorganisms for identification of **antiparasite** drugs

INVENTOR(S): Klein, Ronald P.; Grueby, Timothy J.

PATENT ASSIGNEE(S): Upjohn Co., USA

TYPE: PCT Int. Appl., US, JP

CODEN: PCTINT

DOCUMENT TYPE: Patent

LAW IMAGE: English

PATENT AND DOCUMENT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117260	A1	19911114	WO 1991-US21767	19911425
W: AU, BR, BG, BR, CA, FI, HU, JP, KP, KR, DE, NL, NO, NW, N, PL, PT, SI, SV, US				
RU: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 5179143	A	19920122	US 1990-517633	19900602
AU 9179750	A1	19911127	AU 1991-79750	19910425
PCT INT APPN. INFO.:			US 1990-517633	19900602
			WO 1991-US21767	19911425

AB A method for identifying **antiparasitic** drugs comprises expressing **parasite** gene-complemented microorganisms to the **test** compd. and detg. microbial viability. An *Escherichia coli* mutant deficient in both phosphofructokinase (PFK) **enzymes** was used to clone the PFK cDNA of *Haemonchus contortus* by complementation. The cDNA was sequenced.

11. ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1988:90393 HCAPLUS

DOCUMENT NUMBER: 108:90393

TITLE: A sensitive and efficient isoenzyme technique for small arthropods and other invertebrates

AUTHOR(S): Eastoe, Simon; Boushy, Ian A.

TYPE: JOURN. SOURCE: Reg. Sch. Biol. Sri., Austl. Univ., Canberra, 2611, Australia

TYPE: Bulletin of Entomological Research 1987, 77, 3, 407-15

CODEN: BEREAZ; ISSN: 0007-4653

DOCUMENT TYPE: Journal

LAW IMAGE: English

AB An isoelectrophoretic method for the study of **enzyme** variation, which uses cellulose acetate sheets with an agar overlay for staining, the use of a very good general purpose buffer (citrate-amino-propylglycine), Triton, and the use of sodium azide as a **bacteriocide** to allow

and their structure of known, as solids, are described. Tests are specified in the technique on Tetrahydron Articum Linn., *Artemesia*, and several species of *Brassophila*. The technique offers sensitivity equal to greater than starch or polyacrylamide gel electrophoresis and is applicable to many small organisms, allowing parallel **testing** of similar individuals for different types of **enzymes**. The **testing** of known **enzymes** in *Artemesia* and *Tetrahydron Articum* indicates that the technique is consistent with respect to time and materials, and suitable for analytical methods.

9075-65-4, Glycerol 3-phosphate

1991-1992 學年上學期各科成績

For the first time, the results of the 2010 Census are available online at 2010.census.gov. The Census Bureau has also released the first set of data from the 2010 Census, including population and housing unit counts for the nation, states, and counties.

1. ANSWER IS OF 15 WORDS OR LESS
2. ACCESS NUMBER: 1074-1146-1 HCAPIN
3. DOCUMENT NUMBER: 11115
4. AUTHOR(S): Effects of some antitumor agents on growth and
glycolytic **enzymes** of the flagellate
Crithidia
5. PUBLICATION SOURCE: Raichi, Cyrus J.; Classic, Edward L.; Koren, Iris E.
Haskins Lab., New York, NY, USA
Journal of Bacteriology (1980), 151(1), 23-4
6. PUBLICATION DATE: JOURNAL; ISSN: 0021-9193
7. LANGUAGE: English
8. ABSTRACT: Some antitumor agents known to specifically inhibit certain tumor cell **enzymes** were examd. for activity against glycolytic **enzymes** and for growth of the insect trypanosomatid, *C. fasciculata*. The cytoplasmic **enzymes** hexokinase, α -glycerophosphate dehydrogenase, malic dehydrogenase, and glucose-6-phosphate dehydrogenase were **tested**. Agaricic acid (1-hydroxy-1,2,3-noradecanetricarboxylic acid) was highly inhibitory (50-100 μ M) to malic and α -glycerophosphate dehydrogenases at 10 μ M and 10 μ M, 10 μ M; 2-(p-hydroxyphenyl)-2-phenylpropane (2 μ M) and 5,6-dichloro-2-benzoxazolinone (5 μ M, 10 μ M) were less effective (50-100 μ M) inhibition against them. The antiprotozoal agents primaquine (4 μ M), 10 μ M and Melarsoprol (8 μ M, 10 μ M) were 50-100 μ M inhibitory. Agaricic acid, 2-(p-hydroxyphenyl)-2-phenylpropane, and 5,6-dichloro-2-benzoxazolinone inhibited growth of Crithidia at less than 10 μ M. Eight other **test** compds. from the Cancer Chemotherapy National Service Center (CCNSC) were not toxic to cell growth, although two (4-biphenylcarboxylic acid and 1-(p-chlorobenzyl)-2-ethyl-5-methylindole-3-acetic acid) inhibited Crithidia α -glycerophosphate dehydrogenase below 10 μ M. All of the compds. used specifically inhibited cancer cell α -glycerophosphate dehydrogenase. The corresponding **enzyme** in pathogenic African trypanosomes is important in their terminal respiration. *C. fasciculata* may be useful in preliminary evaluation of chemotherapeutic agents as potential trypanocides.
9075-65-4, α -glycerophosphate dehydrogenase
10. Crithidia fasciculata, neoplasms, insectar, malignant, sp.

Elvittimata tágordatá, neoplasm linijitir aligat or